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Claims

- 1. A targetable diagnostic and/or therapeutically active agent comprising a suspension in an aqueous carrier liquid of a reporter comprising gas filled microbubbles stabilised by monolayers of film-forming surfactant, said agent further comprising at least one vector.
- 2. An agent as claimed in claim 1 wherein the gas comprises air, nitrogen, oxygen, carbon dioxide, hydrogen, an inert gas, a sulphur fluoride, selenium hexafluoride, a low molecular weight hydrocarbon, a ketone, an ester, a halogenated low molecular weight hydrocarbon or a mixture of any of the foregoing.
 - 3. An agent as claimed in claim 2 wherein the gas comprises a perfluorinated ketone, perfluorinated ether or perfluorocarbon.
 - 4. An agent as claimed in claim 2 wherein the gas comprises sulphur hexafluoride or a perfluoropropane, perfluoroputane or perfluoropentane.
- 25 S. An agent as claimed in any of the preceding claims wherein the film-forming surfactant material comprises a non-polymeric and non-polymerisable wall-forming surfactant material, a polymer surfactant material or a phospholipid.
- 6. An agent as claimed in claim 5 wherein at least 75% of the film-forming surfactant material comprises phospholipid molecules individually bearing net overall charge.
- 7. An agent as claimed in claim 6 wherein at least 75% of the film-forming surfactant material comprises one or

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more phospholipids selected from phosphatidylserines, phosphatidylglycerols, phosphatidylinositols, phosphatidic acids and cardiolipins.

- 8. An agent as claimed in claim 7 wherein at least 80% of said phospholipids comprise phosphatidylserines.
 - 9. An agent as claimed in any of the preceding claims wherein the film-forming surfactant material comprises a lipopeptide.
 - 10. An agent as claimed in any of the preceding claims wherein the vector is selected from antibodies; cell adhesion molecules; cell adhesion molecule receptors; cytokines; growth factors, peptide hormones and pieces thereof; non peptide agonists antagonists and non-bioactive binders of receptors for cell adhesion molecules, cytokines growth factors and peptide hormones; pligonucleotides and modified oligonucleotides; DNA-binding drugs; protease substrates/inhibitors; molecules generated from combinatorial libraries; and small bioactive molecules.
- 11. An agent as claimed in any of the preceding claims
 25 wherein the vector or vectors have affinity for targets
 at a level such that the agent interacts with but does
 not fixedly bind to said targets.
- or vectors are selected from ligands for cell adhesion proteins and cell adhesion proteins which have corresponding ligands on endothelial cell surfaces.
- 13. An agent as claimed in any of the preceding claims wherein the vector or vectors are sited such that they are not readily exposed to the target.

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- An agent as claimed in any of the preceding claims 14. wherein the vector is covalently coupled or linked to the reporter.
- An agent as claimed in any of claims 1 to 13 5 15. wherein the vector is coupled or linked to the reporter through electrostatic charge interactions.
- An agent as claimed in any of plaims 1 to 13 16. wherein the vector is coupled or linked to the reporter 10 by means of avidin-biotin and/or streptavidin-biotin interactions.
 - An agent as claimed in any of the preceding claims 17. which further contains motives which are radioactive or are effective as X-ray contrast agents, light imaging probes or spin labels.
 - An agent as claimed in any one of the preceding claims further comprising a therapeutic compound.
- An agent as claimed in claim 18 wherein said 19. therapeutic compound is an antineoplastic agent, blood product,/biological response modifier, antifungal agent, hormone or hormone analogue, vitamin, enzyme, 25 antial/lergic agent, tissue factor inhibitor, platelet inhib/itor, coagulation protein target inhibitor, fibrin formation inhibitor, fibrinolysis promoter, antiangiogemic, circulatory drug, metabolic potentiator, Antitubercular, antiviral, vasodilator, antibiotic, 30 antiinflammatory, antiprotozoan, antirheumatic, narcotic, ppiate, cardiac glycoside, neuromuscular blocker, sedative, local anaesthetic, general anaesthetic or genetic material.
 - An agent as claimed in claim 18 or claim 19 wherein 20. said therapeutic compound is covalently coupled or

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linked to the reporter through disulphide groups.

- An agent as claimed in claim 18 or claim 19 wherein 21. a lipophilic or lipophilically-derivatised therapeutic compound is linked to the surfactant monolayers stabilising the gas-filled microbubbles of the reporter through hydrophobic interactions.
- A combined formulation comprising: 22.
- i) a first administrable composition comprising a 10 pre-targeting vector having affinity for a selected target; and
 - ii) a second administrable composition comprising an agent as claimed in any of the preceding claims, said agent comprising a vector having affinity for said pretargeting vector.
 - A combined/formulation as claimed in claim 22 wherein said pre targeting vector is a monoclonal antibody.
 - A combined formulation comprising: 24.
 - a first administrable composition comprising an agent as claimed in any of claims 1 to 21; and
 - a second administrable composition comprising a substance/capable of displacing or releasing said agent from /its /target.
 - A combined formulation comprising:
- i) a first administrable composition comprising an 30 agent as claimed in claim 20; and
 - a second administrable composition comprising a reducing agent capable of reductively cleaving the disulphide groups coupling or linking the therapeutic compound and reporter in the agent of said first administrable composition.

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- 26. A process for the preparation of a targetable diagnostic and/or therapeutically active agent as defined in claim 1 which comprises either coupling or linking at least one vector to a reporter comprising gas-filled microbubbles stabilised by monolayers of film-forming surfactant or generating gas-filled reporter microbubbles using film-forming surfactant having at least one vector attached thereto.
- 10 27. A process as claimed in claim 26 wherein a therapeutic compound is also combined with the reporter.
 - 28. A process as claimed in claim 27 wherein a therapeutic compound containing thiol groups is linked to thiol group-containing surfactant monolayers stabilising the gas-filled microbubbles of the reporter by reaction under exidative conditions so as to generate disulphide groups
- 20 29. Use of an agent as claimed in any of claims 1 to 21 as a targetable ultrasound contrast agent.
- 30. A method of generating enhanced images of a human or non-human animal body which comprises administering to said body an agent as claimed in any of claims 1 to 21 and generating an ultrasound, magnetic resonance, X-ray, radiographic or light image of at least a part of said body.
- 30 31. A method as claimed in claim 30 which comprises the steps:
 - i) administering to said body a pre-targeting vector having affinity for a selected target; and thereafter
- ii) administering an agent as claimed in any of claims 1 to 21, said agent comprising a vector having affinity for said pre-targeting vector.

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- A method as claimed in claim 31 wherein said pre-32. targeting vector is a monoclonal antibody.
- A method as claimed in claim/30 which comprises the steps:
- i) administering to said body an agent as claimed in any of claims 1 to 21; and thereafter
- ii) administering a substance capable of displacing or releasing said agent from its target.
- 34. A method as claimed in any of claims 30 to 33 wherein said agent further comprises a therapeutic compound.
- A method as glaimed in claim 34 wherein said 15 35. therapeutic compound is covalently coupled or linked to the reporter through disulphide groups, and a composition compri/sing a reducing agent capable of reductively/cleayfing\said disulphide groups is subsequently administered. 20
- A method/for in vitro investigation of targeting by 36. an agent as defined in any of claims 1 to 21 wherein cells expressing a target are fixedly positioned in a 25 flow chamber, a suspension of said agent in a carrier liquid/is/passed through said chamber, and binding of said agent to said cells is examined.
- A method as claimed in claim 36 wherein the flow rate of carrier liquid is controlled to simulate shear 30 rates encountered in vivo.

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